Anatomy of the Digestive Unit

Introduction

Digestion starts in the stomach—mixing the food bolus with acid and pulverizing it to liquid. Digestion is completed in the proximal duodenum, where the enzymatic digestion of chyme is facilitated by the exocrine function of the pancreas and biliary system. The proximal duodenum is foregut-derived. The pancreas, liver, and gallbladder are foregut-derived. They share the same blood supply. The proximal duodenum, the foregut derivatives, complete digestion. The rest of the small intestine—the rest of the duodenum, and the entirety of the jejunum and ileum—is committed to absorption. The rest of the small intestine comes from the midgut and has its own blood supply and its own function. In this lesson, "duodenum" means *proximal duodenum dedicated to digestion and (mostly) perfused by the celiac trunk*.

The gallbladder is discussed with the organ that makes bile—the liver—in the Hepatobiliary island. We are going to discuss bile salts, lipid emulsification, and duodenal signaling here, in the discussion of digestion and absorption, but a detailed discussion of the gallbladder comes later in the course. The duodenum receives chyme from the stomach. It then dispatches hormonal signals to inform the exocrine pancreas and gallbladder that their services are needed. Bile (from the gallbladder) and pancreatic juices (from the pancreas) mix with the chyme in the duodenum. That's chemical digestion. The intestines use churning (sequential, aperistaltic contractions, just as in the stomach) to mix the chyme with the digestive juices. **Terminal digestion** occurs at the apical domain of enterocytes, so technically digestion is completed along the length of the small intestine. But that is the digestion of small polymers into their monomers. This lesson is about the macroscopic digestion of chyme—macronutrients—into those smaller polymers.

Anatomy and Blood Supply of the Organs of Digestion

The proximal duodenum, pancreas, and gallbladder represent a singular digestive unit. The stomach did start chemical digestion and pulverized the food bolus into liquid chyme, delivering liquid chyme to the duodenum in small doses. So, although the digestive unit handles only a minuscule amount of chyme at any one time, it is responsible for enabling both terminal digestion and absorption at the intestinal brush border. Because the gallbladder and bile are discussed in the Hepatobiliary island, most of this lesson's discussion is about the duodenum and pancreas. You cannot tell just how closely connected, anatomically, the digestive unit is on a transverse section. We show it here so that you will recognize it in transverse sections on CT or MRI. We then follow with an illustrated discussion of the anatomy and vasculature of the duodenum and pancreas to facilitate your mastery.

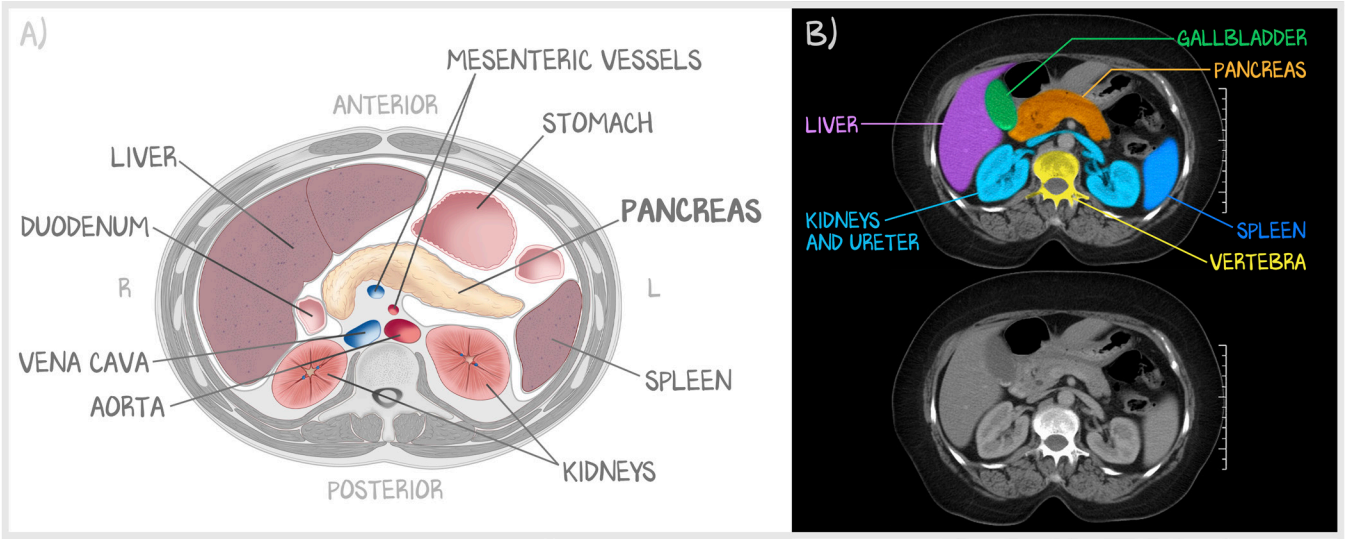

Figure 7.1: Orientation of the Pancreas in the Abdomen
The body of the pancreas is posterior to the stomach, and the tail of the pancreas is anterior to the spleen. The neck and head of the pancreas wrap around the superior mesenteric vein and abut the vena cava and aorta. This is shown in a schematic to the left and nonconctrasted CT scan to the right. Because the pancreas wiggles in between so many planes, it's hard to get one good slice of it.

The **pancreas** has four sections: the head, neck, body, and tail. The tail is free-floating out near the spleen, and the body is behind the stomach, with the head tucked into the fold of the duodenum. This orientation is quite purposeful: the largest part of the pancreas is in maximal contact with the organ it releases its digestive juices into—the proximal duodenum. The head of the pancreas is nuzzled right up to the duodenum. The pancreas has two ducts through which it can release pancreatic juice. The **main pancreatic duct** (it has an eponym that we're not teaching you) merges with the common bile duct (from the gallbladder) to form the **hepatopancreatic ampulla** (eponym: ampulla of Vater). Most of the pancreas is dedicated to exocrine function (the endocrine functions are discussed in the Endocrine module, and the cells of the endocrine function represent a fraction of the organ's cells). The pancreas is almost entirely dedicated to making digestive enzymes and the bicarbonate-rich fluid those enzymes travel in. The majority flows through the main pancreatic duct to the hepatopancreatic ampulla. On the duodenal side, there is the papilla of Vater, separated from the ampulla by the **hepatopancreatic sphincter** (aka the sphincter of Oddi), which opens to allow bile and pancreatic juice to spill into the duodenum. There is also an accessory pancreatic duct, which bypasses the biliary system to drain directly into the duodenum through the minor papilla.

Being nestled up to the duodenum, it is probably not surprising that the pancreas and duodenum share much of their vascular supply. The pancreaticoduodenal arteries form an anastomosis. The **inferior pancreaticoduodenal** artery ascends from the superior mesenteric artery, the next major branch of the aorta after the celiac trunk. The **superior pancreaticoduodenal** artery descends from the gastroduodenal artery that you learned about in the Stomach lessons. That feeds the **head of the pancreas**. The tail gets a different vascular supply. These arteries are lower-yield for examinations, but are what enable the Whipple procedure (GI: Digestion and Absorption: Start to Finish #10: *Pancreatic Pathology*) to be effective in treating cancer of the head of the pancreas—the tail and head are connected by the pancreatic duct but are kept almost entirely separate from the other's vascular supply. The tail is fed by pancreatic branches of the **splenic artery** and a branch of the splenic artery, the **dorsal pancreatic artery**. Don't learn any more branches than that unless your instructors advise it.

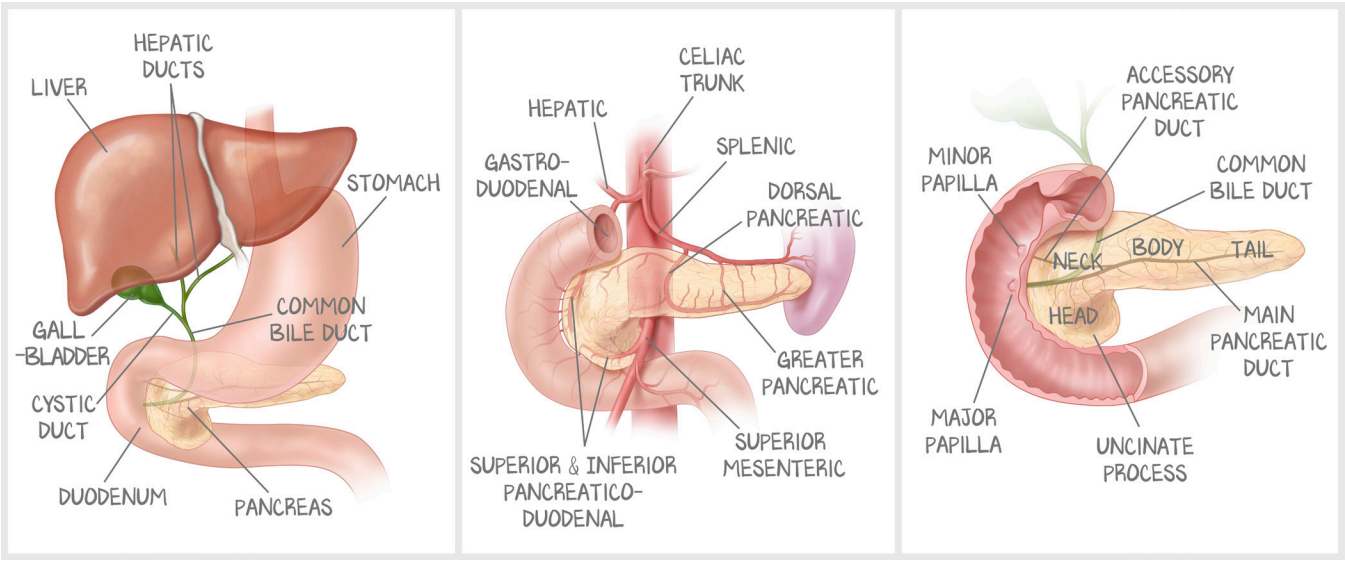

Figure 7.2: Pancreas Anatomy and Relation to the Biliary System
The goals are to demonstrate the relative anatomy. First, to explain how the proximal duodenum and head of the pancreas are intimately related. Second, to demonstrate the vascular supply of the pancreas, coming primarily from the celiac trunk (via the splenic artery and gastroduodenal artery) and a little from the superior mesenteric artery (via the inferior pancreaticoduodenal artery). Finally, to delineate the pancreas into four sections: the head, neck, body, and tail.

The **duodenum** is described in thirds. The first third is perfused by the celiac trunk, **duodenal branches of the gastroduodenal artery**, and what the gastroduodenal artery becomes—the **superior pancreatoduodenal artery**. The remaining two-thirds are perfused by branches of the superior mesenteric artery. The second third is fed by the **inferior pancreaticoduodenal artery** and the final third by the duodenal branches of the **first jejunal artery**. The duodenum is a hollow tube with infoldings of the mucosa that invaginate into the lumen; the folds are called plicae circulares.

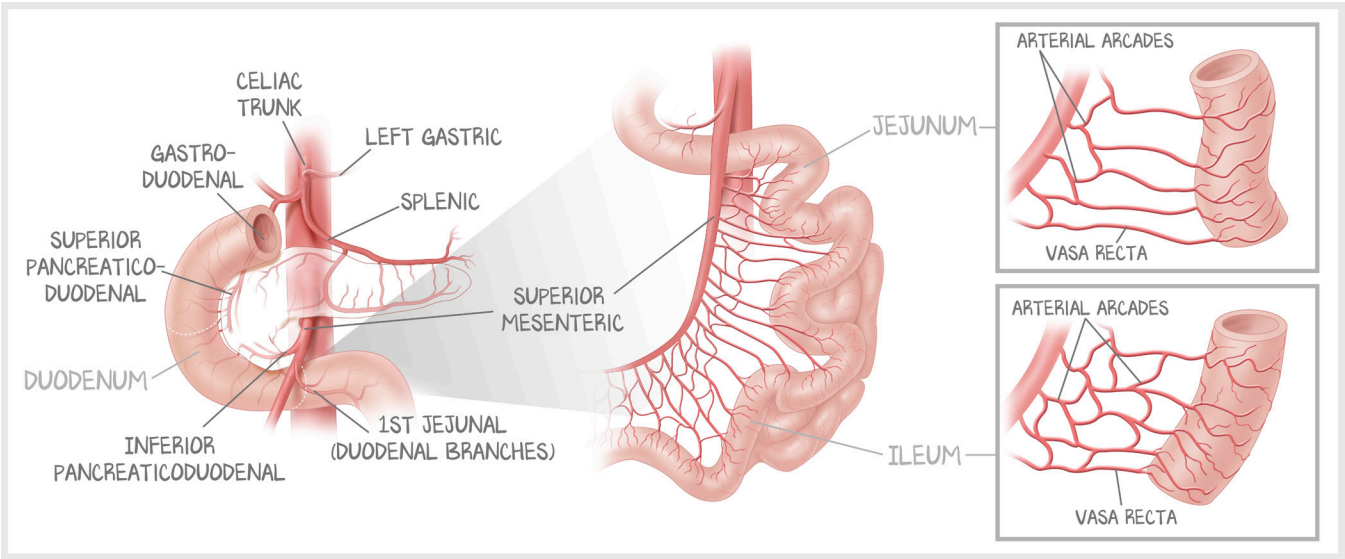

Figure 7.3: Vascular Arrangement of the Duodenum
With the pancreas ghosted from the image, the vasculature of the duodenum can easily be appreciated. The gastroduodenal and superior pancreaticoduodenal arteries irrigate the first third of the duodenum, then the inferior pancreaticoduodenal from the superior mesenteric artery irrigates the second third, and the first jejunal branch irrigates the distal third. In the center, note how the superior mesenteric artery irrigates the entirety of the remaining small intestine. There is also a change from short arterial arcades (anastomoses) and long vasa recta early on to long arcades (anastomoses) and short vasa recta distally.

The GI tract below the diaphragm is divided into three segments: foregut, midgut, and hindgut. The gallbladder, stomach, proximal third of the duodenum, and almost all of the pancreas are all supplied by the same aortic branch (**celiac trunk**), referred to as the **foregut**, and responsible for **digestion**. The distal two-thirds of the duodenum, the jejunum, ileum, ascending colon, and proximal two-thirds of the transverse colon are all supplied by the same aortic branch (**superior mesenteric artery**), referred to as the **midgut**, and mostly responsible for **absorption**. That means that the duodenum is responsible for both digestion and absorption. Sort of. Histologically, yes, it is. But embryologically and by the vasculature? The proximal duodenum is an organ of digestion; the distal duodenum is an organ of absorption. The distal third of the colon, rectum, and anal canal are all supplied by the same aortic branch (**inferior mesenteric artery**) and referred to as the **hindgut**.

The **foregut** is everything from the **esophagus to the first third of the duodenum**, just distal to the hepatopancreatic ampulla, the connection to the biliary system. That means that the pancreas, gallbladder, and liver will be included in the foregut. They all developed alongside the common vascular supply of the foregut, the **celiac trunk**. All of the foregut structures are endoderm-derived and fed by the celiac trunk, except the spleen (the spleen is mesoderm-derived but still gets its vascular supply from the celiac trunk, and its splenic artery feeds the endoderm-derived pancreas). The **midgut** is everything from the first third of the duodenum to the second third of the transverse colon. It is supplied by the **superior mesenteric artery**. The hindgut is everything from the distal third of the colon to the anal canal above the pectinate line—more on this in the large intestine lesson. It receives blood from the inferior mesenteric artery.

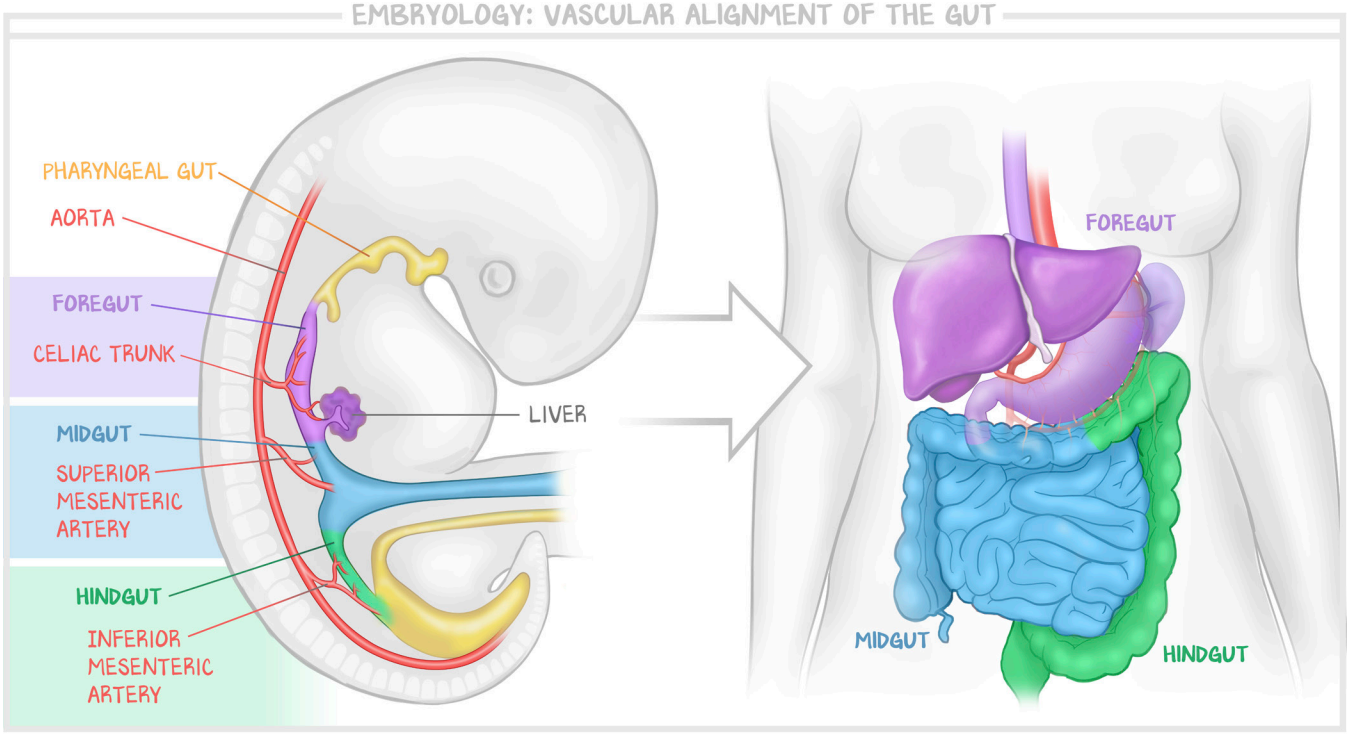

Figure 7.4: Embryology and Vascular Assignment of the Gut
Strong vascular associations can be made—foregut with the celiac trunk, midgut with the superior mesenteric artery, hindgut with the inferior mesenteric artery. Additionally, loose cognitive associations can be made in terms of their functions—foregut does digestion, midgut does absorption, hindgut expels stool.

The **gallbladder** is connected to the duodenum via the hepatopancreatic ampulla, which it shares with the pancreas. It is formed from the foregut and irrigated by the celiac trunk. Its artery comes from the proper hepatic artery. The gallbladder stores bile made by the liver and secretes it into the lumen of the common bile duct, which travels down to the hepatopancreatic ampulla and out through the hepatopancreatic sphincter.

Pancreatic Embryology and Embryologic Failure

The pancreas is endoderm-derived and part of the foregut. It forms as part of the common hepato-pancreatic-biliary bud. But it starts as two separate buds. The smaller **ventral** pancreatic bud is already attached to the common bile duct and will form the **uncinate process**. For the pancreatic duct of the adult pancreas to connect to the biliary tree, the hepatopancreatic ampulla, the ventral pancreatic bud—with the biliary tree attached—needs to fuse with the larger dorsal pancreatic bud and its pancreatic duct. The larger **dorsal** pancreatic bud is directly connected to the duodenum. No matter what the ventral bud does, the dorsal bud is going to become the majority of the pancreas and contain the main pancreatic duct. But . . . that pancreatic duct should mostly connect to the hepatopancreatic ampulla with the common bile duct. To make that happen, the ventral bud is supposed to be spun by the rotation of the stomach posteriorly to the duodenum. While being spun, it holds onto the biliary tree. The two buds meet and fuse. The dorsal pancreas never loses its original connection to the duodenum but also fuses a portion of the pancreatic duct to the common bile duct.

The ventral pancreas becomes the **uncinate process**. The dorsal pancreas becomes the **body and tail of the pancreas**. Their fusion results in the **head** of the pancreas.

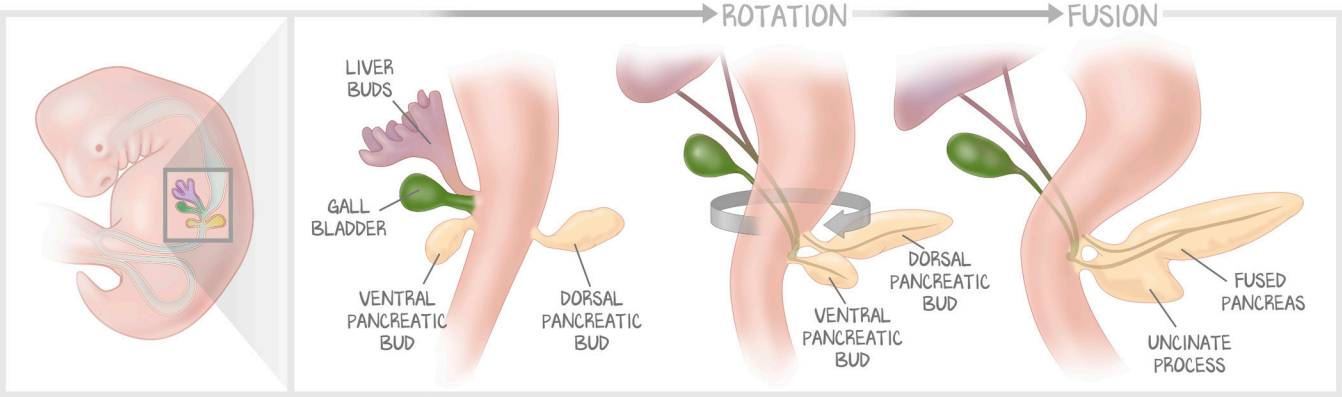

Figure 7.5: Normal Embryology of the Pancreas
The smaller ventral pancreatic bud carries with it the common bile duct, whereas the larger dorsal pancreatic bud develops the bulk of the pancreas and is already connected to the duodenum. The posterior movement of the ventral bud causes the two buds to collide and fuse. The ventral bud becomes the lesser part of the adult pancreas—the uncinate process and part of the head—whereas the dorsal bud becomes the greater part of the pancreas—tail, body, and the other part of the head. But it is the ventral bud that brings with it the common bile duct to fuse with the pancreatic duct, enabling the best flow of pancreatic juices from the larger dorsal pancreatic bud through the hepatopancreatic ampulla.

The ventral pancreas is supposed to swing around the back of the intestine with the biliary tree, leaving an intestine without anything on top of it in the front. The ventral-bud-portion-attached-to-the-biliary-tree is going with the biliary tree. It will smoosh with the dorsal bud and become the uncinate process. But if the ventral pancreas doesn't behave (e.g., there are two buds that grow in both directions), then what could happen is an **annular pancreas**, a pancreas wrapped all the way around the duodenum. This can cause the appearance of duodenal atresia, or at least duodenal stenosis, and so presents identically to

duodenal atresia, except that annular pancreas is not associated with Down syndrome. Duodenal atresia is discussed below.

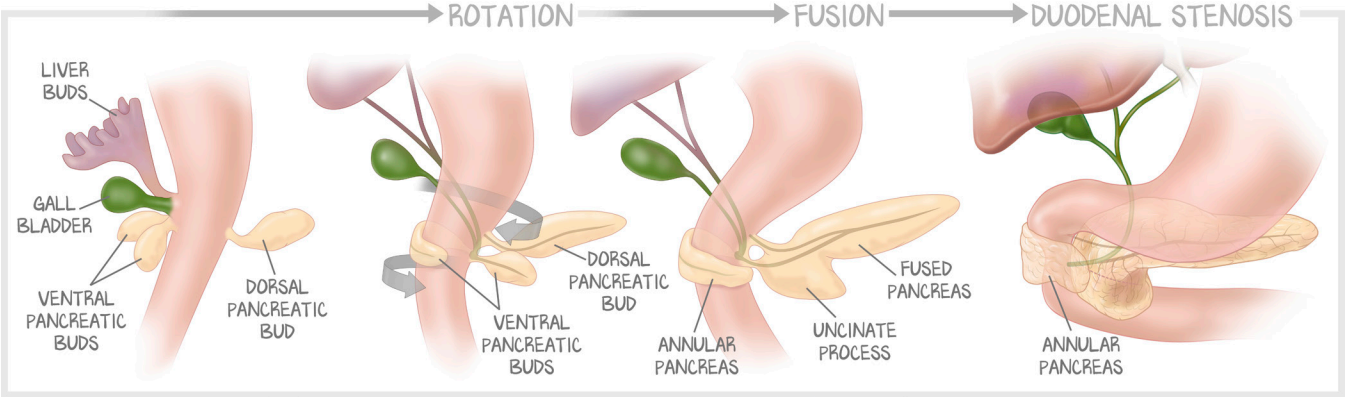

Figure 7.6: Development of Annular Pancreas
Annular pancreas can occur as a result of a misbehaving ventral bud. Especially if there are two ventral buds, and one grows the wrong way. Although the normal ventral pancreatic bud is rotated by the twisting of the stomach and bile duct, the other ventral bud either doesn't rotate or grows the wrong way. The result is a complete ring of pancreas choking off the duodenum, resulting in complete atresia (or at least stenosis).

The most common embryologic finding is **pancreas divisum**. In this condition, the ventral and dorsal buds fuse just fine, but the ducts don't. That leaves the bulk of the pancreas (all of the dorsal pancreatic bud's derivatives) connected to the smaller duct that leads to the minor ampulla, and the minority of the pancreas (all of the ventral pancreatic bud's derivatives) connected to the larger duct, which merges with the common bile duct. More tissue draining through a smaller space is thought to be one cause of pancreatitis. Pancreas divisum may have no symptoms at all and is present in up to 10% of the population.

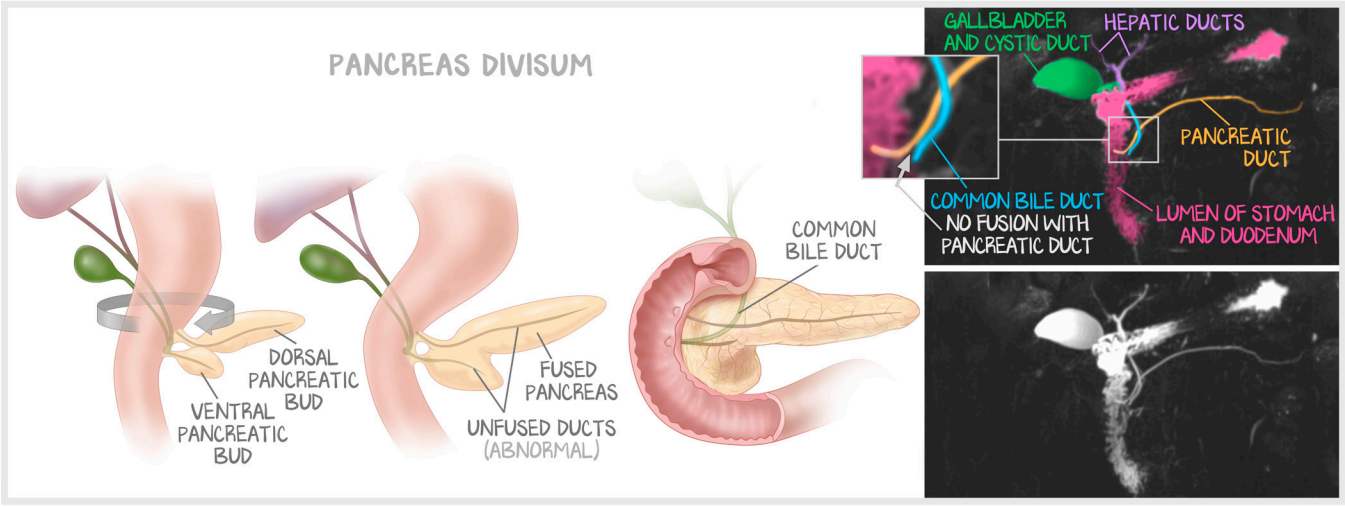

Figure 7.7: Pancreas Divisum
This figure combines several serial MRIs to create a three-dimensional representation of the ducts, demonstrating pancreas divisum (the large pancreatic duct is separate from the common hepatic duct) and introducing the anatomy of the ducts and the organs that secrete into them. The color-coded versions are provided alongside non-color-coded versions so that you can examine the unlabeled images.

Histology of the Exocrine Pancreas

The structure of the pancreas reflects that it is both an endocrine organ (glucagon, insulin) and an exocrine organ. Most of the organ is made for its exocrine function. Endocrine cell islets can be seen scattered sporadically throughout the pancreas, usually near blood vessels (into which they secrete hormone). The rest of the exocrine pancreas is arranged into acini, clusters of acinar cells around a duct. This is our focus. It is an exocrine gland. **Acinar cells** synthesize and store digestive enzymes in **zymogen granules**. When instructed to do so, these acinar cells undergo exocytosis, releasing their zymogens into the acinar ductules. Ductules become ducts, and ducts eventually feed the main pancreatic duct. This ductal system carries the zymogens to the confluence with the common bile duct and, finally, to the small intestine.

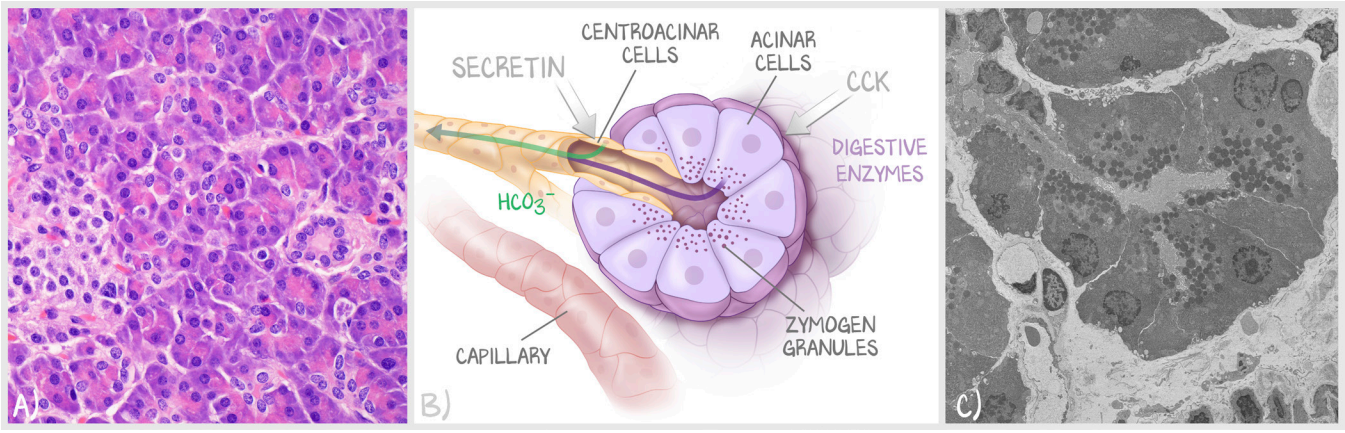

Figure 7.8: Histology of the Exocrine Pancreas
Successive magnifications of pancreas histology. In the first, the connective tissue that separates the lobules and a single, pale-staining islet of Langerhans provide context for the remainder of the images. Essentially, the pancreas is entirely composed of acini punctuated by islets of Langerhans, which provide the pancreas' endocrine function. In the next magnification, an intralobular ductule is seen amongst the acini, and an interlobular ductule, interlobular venule, and interlobular arteriole are seen in the connective tissue nearby. The third panel shows the ductule in more detail, and the final magnification shows a single acinus separated from other nearby acini by white space (an artifact of preparation that conveniently demonstrates which cells are attached to one another—those with nuclei toward the outside of the acinus, near the white space).

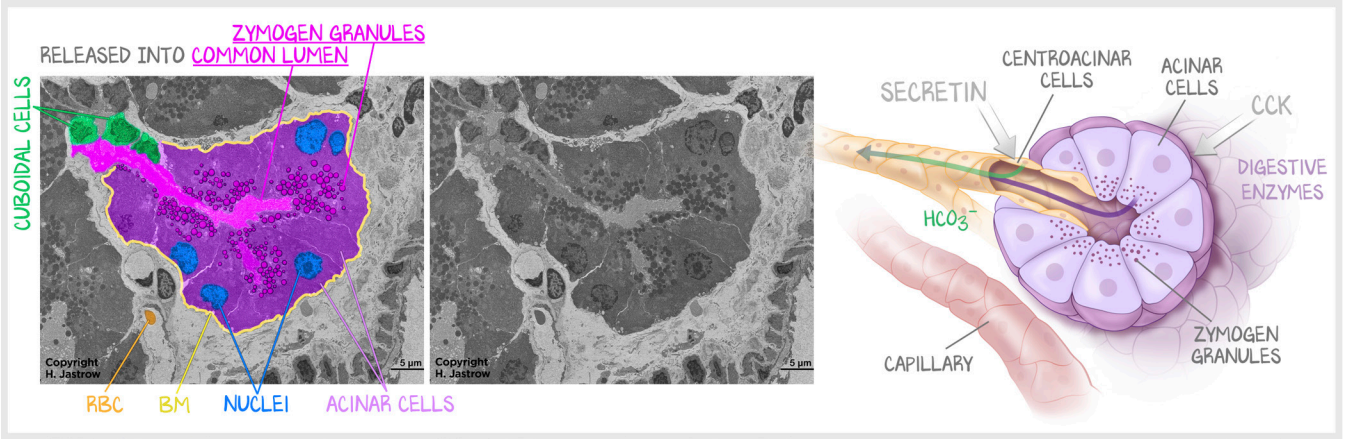

Figure 7.9: Exocrine Pancreas Acinus
(a) Electron micrograph demonstrating the multiple columnar cells of a single acinus, the visible nuclei against the connective tissue outside the basement membrane, and the zymogen granules concentrated at the apical domain of the cells and being released into a common lumen. At the end of the acinus, the cells transition from columnar to cuboid as the ductular cells become the lining of the ductules. (b) Artist's rendition of a single acinus, illustrated to match the accompanying electron micrographs.

Zymogens are **inactive precursors of digestive enzymes** that are activated by trypsin once in the duodenum. Zymogens are released into ducts and flushed into the duodenum. Those ducts begin with **centroacinar cells**, the lining of the smallest duct structure within the acinus. They are histologically and functionally the same as **ductal cells**, which line the ductules and, eventually, the large ducts. Ductal cells **secrete bicarbonate** and **water** to form the pancreatic secretions and flush the zymogens released by acinar cells. Ductal cells also secrete **trypsin inhibitor** into the pancreatic secretions. **Secretin** from S cells in the duodenum signals the secretion of pancreatic juice—water and bicarb. **CCK** released from I cells of the duodenum stimulates gallbladder contraction, pancreatic juice secretion, and the exocytosis of zymogens.

Histology of the Duodenum (Not the Small Intestine)

The histology of the duodenum reflects its absorptive nature rather than its digestive nature. The physiology of digestion (discussed in the next lesson) stimulates the release of bile and pancreatic juice for chemical digestion. In this discussion, we're going to talk about the duodenum specifically, but as you'll see in the next lesson, the features of **villi** and the **brush border** will continue along the length of the small intestine. Because we want to focus on terminal digestion and absorption physiology in the next lesson, we're going to talk about duodenum histology in this lesson, then use that information in the next lesson to build out the rest of the small intestine.

The duodenum is the first segment of the small intestine. It is the site of greatest absorption (the greatest concentration of food is delivered from the stomach, being first) and the site of chemical digestion as it sends signals to and receives juices from the pancreas and gallbladder. It houses the cells that send those signals and also the cells that inhibit the stomach in order to buy time for chemical and mechanical digestion in the duodenum.

The small intestine—duodenum, jejunum, ileum—are part of the gut tube, so they have the familiar histologic layers that you've learned so far: mucosa, submucosa, muscularis externa, and adventitia covered in the mesothelium of the peritoneal cavity (serosa). We'll talk about the features that enable a histologic diagnosis of each segment of the small intestine in the next lesson. Here, we introduce the concept of crypts, villi, and the cells of the simple columnar epithelium.

Like the stomach, the small intestine has a tall mucosa that enables epithelial invaginations into the lamina propria called intestinal glands. These are also referred to as **crypts of Lieberkühn**. Invagination, gland, and crypt are all used to describe these invaginations and are used interchangeably in other texts. Because the physiology is so unlike that of the gastric glands (gastric invagination of epithelium), we are going to use the word "crypt" (intestinal epithelial invaginations) exclusively for the intestines, and "gland" exclusively for the stomach. At the **base** of the crypts are **stem cells**. Stem cells divide and differentiate a daughter cell. That daughter cell is committed to becoming one of the cell types of the epithelium. These cells migrate by being pushed one cell higher by the next stem cell division. Until they reach terminal differentiation into an enterocyte, goblet cell, Paneth cell, or M cell, this new daughter cell is an **intermediate cell**, which undergoes further divisions as it ascends the height of the crypt towards the intestinal lumen, pushed up by the proliferation of the stem cells within the crypt below.

When these cells reach the surface of the crypt, they aren't done ascending. The defining characteristic of the intestinal mucosa is the presence of villi. **Villi** are evaginations of the mucosa. The lamina propria extends off the surface of the crypt and into the lumen. The lamina propria is still the lamina propria, containing blood vessels, lymphatics, nerves, and immune cells. And that lamina propria is separated from the epithelium by a basement membrane. The epithelium is **simple columnar**. The cells of the epithelium continue to migrate towards the tips of the villi, where the oldest cells are. There, the eldest slough off into the lumen to be expelled with the stool, with new cells emerging from the crypts to take their place.

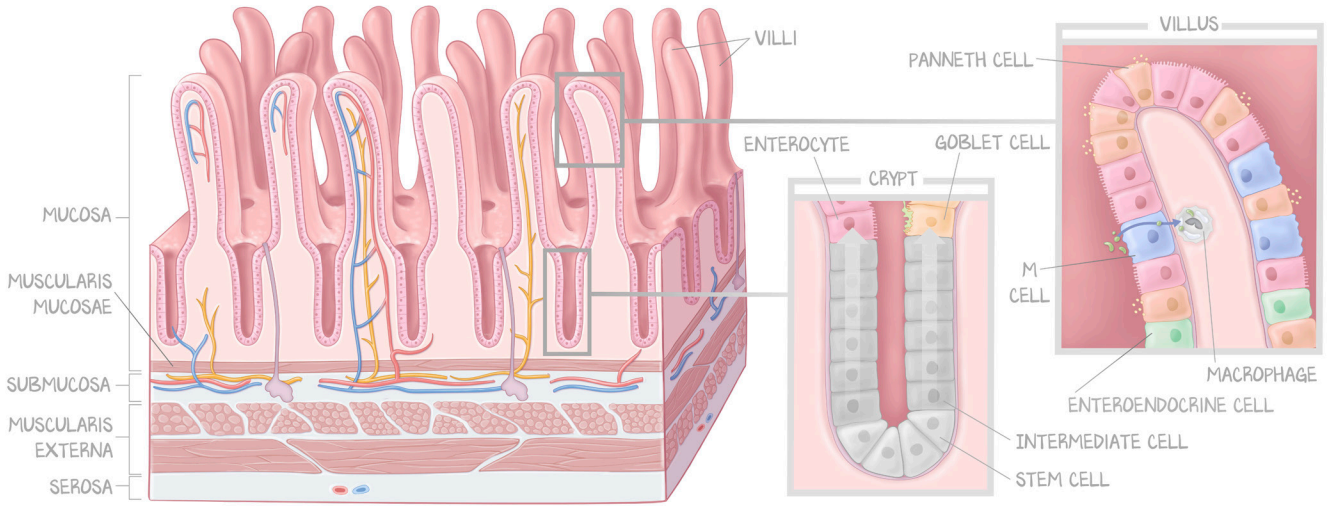

Figure 7.10: Crypts, Villi, and Cells
The epithelium is a simple columnar epithelium. However, the mucosa is not simple. Like the stomach, there are invaginations of the epithelial layer into the lamina propria, bound by the muscularis mucosae. In the stomach, they are called glands. In the intestine, they are called crypts. At the base of the crypts are stem cells. The crypts are lined with mitotically active, not-terminally differentiated intermediate cells. The villus begins at the theoretical surface of the crypts, the epithelium of the crypts being continuous with the epithelium of the villi. These evaginations into the lumen maximize the absorptive surface area. Within the epithelium of each villus are enterocytes, goblet cells, M cells, Paneth cells, and enteroendocrine cells. This illustration should serve as a visualization of the surrounding text and prepare you to interpret the histology that follows.

Enterocytes (enteric cells) serve as the absorptive cells of the small intestine. They have **microvilli** on their apical domain, which maximally enhance their surface area. Embedded in the plasma membrane of those microvilli are digestive enzymes (terminal digestion of small polymers) and transporters of absorption (absorption of digested small polymers). We'll cover these in detail in the next lesson.

Enteroendocrine cells were discussed in GI: Digestion and Absorption: Start to Finish #5: *Physiology and Pharmacology of the Stomach*. They secrete hormones in response to luminal contents. The two that matter most to digestion are the S cells (secrete secretin) and the I cells (secrete CCK). These are the enterogastrone-secreting cells.

Goblet cells secrete mucus. They are the same mucin-secreting goblet cells you've seen before. They appear as white blobs in the epithelium.

M cells are experts at mass transport. They phagocytose luminal contents—bacteria, antigens, large molecules—and pass them through the epithelial layer without enzymatic degradation. The epithelium is a simple columnar epithelium held together by desmosomes and sealed by a zona adherens. This means that paracellular transport is severely restricted to ensure that all the absorption is performed by enterocytes. And to be absorbed, enzymatic digestion must occur first. But M cells are the surveyors of the intestine. They don't require the things they bring across the epithelium to be digested. Instead, they immediately pass whatever they ingest to resident macrophages (called dendritic cells, but we call them resident macrophages because their other name sounds too much like dendrite). In this fashion, M cells enable these resident macrophages to constantly sample the antigens in the lumen without exposing the macrophages to an overwhelming number of antigens.

Paneth cells regulate the gut microbiome. They secrete enzymes that degrade certain bacteria but not others. They matter to the health of the intestine. We don't know a lot about them, and they aren't the target of disease or treatment, so this is the only mention they get.

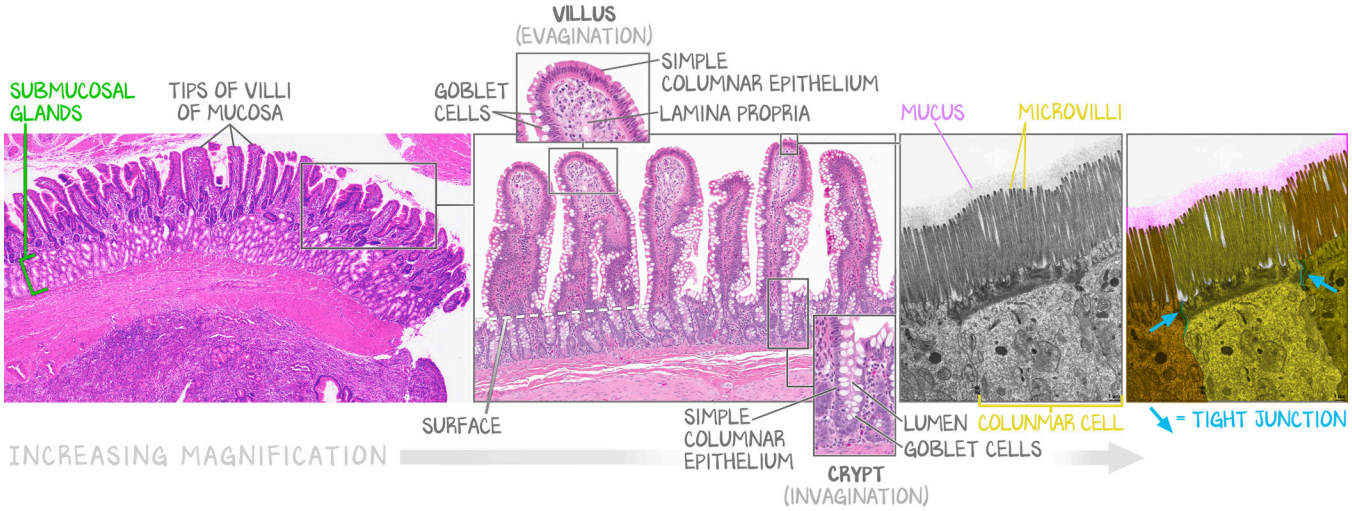

Figure 7.11: Villi and Microvilli
The left panel shows a low-powered view demonstrating the relative sizes and locations of the layers of the GI tract in the duodenum—the mucosa has villi, the submucosa has glands, and the muscularis lies beneath. The details of the villi and crypts cannot be fully appreciated at such a low magnification. In the next panel, at a higher magnification, the details of the villi, crypts, and surface are more apparent. Villi are evaginations of the lamina propria, lined with simple columnar epithelium that is continuous with that of the invaginations into the crypts. The electron micrograph shows the brush border, the microvilli that top the villous columnar cells. Only the absorptive cells and the protective periciliary mucus can be seen at this high magnification, whereas numerous mucin-secreting goblet cells (anything white other than the lumen) can be seen on light microscopy. The EM also shows the zona adherens at the apical edge of neighboring cells' lateral domain, and the actin filament anchors can be seen on the apical aspect of the enterocytes below the plasma membrane.

Duodenal Embryology and Embryologic Failure

All of the gut tube is derived from **endoderm**, and the duodenum is no different. The gut tube begins as a hollow tube, fills in the hollow space with cells, and then becomes a hollow tube again through apoptosis. The filling and apoptosis are required to make the villi and the plicae circulares (you won't see this term again). The gut tube forms first by the proliferation of endoderm from the outside of the tube in. By week 6, the lumen is entirely occluded, filled in by cells. **Recanalization** is the process by which epithelial cells undergo apoptosis to restore the gut lumen. If there is a failure of recanalization, **stenosis**, wherein the lumen is patent but narrowed, or **atresia**, wherein there is no recanalization at all, can occur.

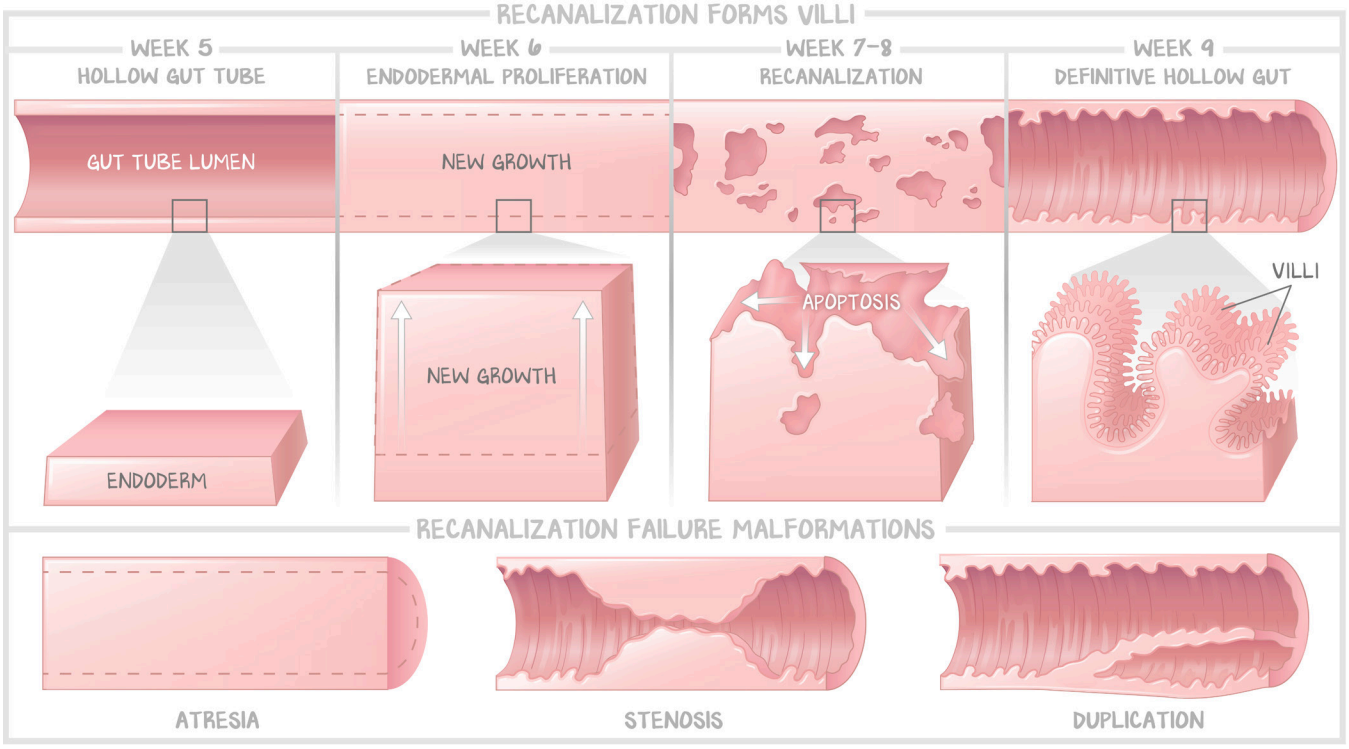

Figure 7.12: Recanalization Forms Villi
The gut tube begins as a hollow tube lined with endoderm. By week 6, the proliferation of the endodermal lining occludes the gut lumen. It must be filled in so that the final structure—villi atop plicae circulares—can be chiseled out. Recanalization is usually completed by week 9. Recanalization can go awry. Incomplete recanalization results in stenosis. A lack of recanalization results in atresia. Atresia distal to the pancreatic duct results in bilious emesis. Atresia proximal to the pancreatic duct results in nonbilious emesis.

During development, the fetus swallows the amniotic fluid. Baby swallows the fluid, absorbs the water, and urinates it back out as amniotic fluid. Baby also receives nutrients from mom through the umbilical vein. If baby has an atretic lumen, baby has an effective intestinal obstruction and that amniotic fluid cannot be absorbed. But because baby still gets nutrients from mom via the umbilical veins, baby gets blood—fluid—which is filtered by the fetus's intact filtering system (more on this in Renal), so baby still urinates. The same amniotic fluid is produced, but less is swallowed and absorbed, resulting in more amniotic fluid overall. This results in **polyhydramnios** in utero.

When baby is born, baby will swallow air with the first few breaths. Therefore, air should be in the GI tract. Not a lot, but enough to create a bowel gas pattern. Gas will be in the gut tube until it is passed, released as a baby fart. Toot. But if air can't get from the mouth to the rectum, air is going to accumulate, and baby's intestines will be full of air. If the atresia is in the proximal duodenum, the bile is made and excreted without difficulty, past the atretic segment, but air cannot reach the ampulla. Baby will have nonbilious vomiting and a belly full of air on X-ray called a **double bubble sign**—air in the stomach and air in the first part of the duodenum. But oh wait, drat, there are three thirds to the duodenum. If the duodenum is atretic distal to the hepatopancreatic ampulla, then bile can't get to the distal GI tract, and the baby will have **bilious emesis**. So what to learn? Because this disease is considered in the context of other baby emesis syndromes, you should know that it can present with bilious or nonbilious emesis, but because pyloric stenosis presents with nonbilious emesis and annular pancreas (the other double bubble disease, discussed above) presents with bilious emesis, you should learn that **duodenal atresia causes double bubble and bilious emesis** just like annular pancreas does. Duodenal atresia is associated with Down syndrome.

Citation

Figure 7.1: Courtesy of Radiopaedia.org.

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